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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/802,796
Filing Date: March 18, 2004
Appellant(s): COLE ET AL.

Lisa M. Matovcik
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 11, 2008 appealing from the Office action mailed March 17, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (2001).

Revised Interim Utility Guidelines Training Materials, Synopsis, p. 3-8 (1999).

Written Description Training Materials, Revision 1, March 25, 2008, Example 13, p. 45, citing Kabat, EA, Structural Concepts in Immunology and Immunochemistry, 2nd Ed, (1976).

Philipp et al, "PHYSICAL MAPPING OF *MYCOBACTERIUM bovis* BCG PASTEUR REVEALS DIFFERENCES FROM THE GENOME MAP OF *MYCOBACTERIUM tuberculosis* H37Rv AND FROM *M. bovis*" Microbiology, 142: 3135-3145, 1996.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejection-35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 51-54 and 57 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by a substantial asserted utility or a well-established utility. The specification suggests but does not demonstrate that the claimed polypeptides have GDP-D-mannose dehydratase activity based on a 51% homology with a GDP-D-mannose dehydratase from another organism. Neither the specification nor the art describe the significance of this activity or a real world use for a protein with this activity.

Rejection-35 U.S.C. 112, 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-54 and 57 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or which it most nearly connected, to use the invention. Specifically, since the claimed invention is not supported by a substantial utility for the reason set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

(10) Response to Argument

Appellant's Arguments

For the rejection under 35 U.S.C. 101 of lack of utility, Appellant argues that *M. bovis*, a strain of the bacteria that infects cattle, is commonly used to vaccinate humans against tuberculosis. Appellant argues that distinguishing between *M. tuberculosis* and *M. bovis* "in a biological sample identifies individuals infected with *M. tuberculosis* as distinct from those vaccinated with *M. bovis*." Appellant argues that "the claimed polypeptides are useful for distinguishing *M. tuberculosis* from *M. bovis*…one of the polymorph regions, a 12.7 kb region of SEQ ID NO: 1, contains eleven open reading frames…" Appellant argues that "assuming that some of the gene products from this region represent proteins with antigenic properties, it could be possible to develop a test that can reliably distinguish between the immune response induced by vaccination with *M. bovis* BCG vaccine strains and infection with *M. tuberculosis*." Appellant makes

reference to the Written Description Training Materials, Revision 1, March 25, 2008, Example 13, that "according to the Office, this assumption is well-grounded. 'Early studies empirically established that proteins were good antigens when injected into a species other than the one from which they originated.'" Appellant argues that "the claimed proteins act as antigens, which can be detected by conventional immunoassays. Their presence indicates the presence of *M. tuberculosis* regardless of whether or not *M. bovis* is present in the sample."

Appellant argues that "the claimed polypeptides have a substantial, real world, utility simply as a consequence of their differential expression by mycobacterial strains." Appellant makes reference to Philipp et al, indicating that more than two billion people worldwide have been immunized with the attenuated *M. bovis* BCG and test positive in assays for the presence of mycobacteria." Appellant further argues that "these vaccinated subjects do not, however, test positive in assays for the claimed polypeptides unless they are also infected with *M. tuberculosis*."

Appellant argues that "the facts asserted by Appellant, e.g., that the claimed polypeptides are encoded by a region of the genome present in one strain but not the other, logically support the asserted utility of using them to distinguish *M. tuberculosis* from *M. bovis*."

Further, Appellant argues that "it is critical to understand that the asserted utility is independent of any homology to GDP-D-mannose dehydratases. This utility derives from the selective presence of one or more claimed polypeptides in one strain of

Mycobacterium compared to another strain, and the ability of a conventional assay to distinguish the two strains by the mere presence (or absence) of the polypeptide."

Appellant argues that "the Examiner failed to consider Appellant's response to the rejection" in that "[R]egardless of the function of the encoded polypeptide...the claimed polynucleotide sequence of the invention had utility simply as a consequence of its expression by *M. tuberculosis*, but not *M. bovis* BCG."

Finally, Appellant argues that "the enablement rejection is improper because the utility rejection is improper."

Response to Arguments for Utility

In order to establish utility, the claimed invention must be specific and substantial. MPEP states the following: "35 U.S.C. 101 serves to ensure that patents are granted on only those inventions that are "useful"…Deficiencies under the "useful invention" requirement of 35 U.S.C. 101 will arise in one of two forms. The first is where it is not apparent why the invention is "useful". This can occur when an applicant fails to identify any specific and substantial utility for the invention or fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention." For specific utility, the MPEP states the following: "A specific utility is specific to the subject matter claimed >and can "provide a well-defined and particular benefit to the public."…This contrast with a general utility that would be applicable to the broad class of invention…For example, indicating that a compound may be useful in treating unspecified disorders, or that the

compound has “useful biological” properties, would not be sufficient to define a specific utility for the compound…Similarly, a claim to a polynucleotide whose use is disclosed simply a s a “gene probe” or “chromosome marker” would not be considered to be a specific in the absence of a disclosure of a specific DNA target” (see MPEP 2107.07 A, “Specific Utility"). Furthermore, the MPEP states that “[A]n application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research…an asserted use must show that the claimed invention has a significant and presently available benefit to the public” (see MPEP 2107.01 B “Substantial Utility").

In the instant case, it is noted that Appellant is using speculative language to describe the utility of the claimed polypeptides. Throughout the specification, Appellant uses the words, “could be”, “can be”, “may be” to establish utility for the claimed polypeptides. For example, the specification discloses that "this polynucleotide of interest contains 11 ORFs that may be involved in polysaccharide biosynthesis" (see paragraph [0063] of instant specification 2005/0250104 A1); “such a polynucleotide of interest may be used as a probe or a primer useful for specifically detecting a given mycobacterium of interest, such as *Mycobacterium tuberculosis* or *Mycobacterium bovis* BCG” (see paragraph [0069] of instant specification as above).

In the instant case, Appellant has not established specific utility. As described above, when establishing specific utility, Appellant uses the words, “may be”, “could be” and “can be”. For example, the specification discloses that “it could be possible to develop a test that can reliably distinguish between the immune response induced by

vaccination with *M. bovis* BCG vaccine strains and infection with *M. tuberculosis*"; "this polynucleotide of interest contains 11 ORFs that may be involved in polysaccharide biosynthesis" ; "such a polynucleotide of interest may be used as a probe or a primer useful for specifically detecting a given mycobacterium of interest, such as *Mycobacterium tuberculosis* or *Mycobacterium bovis* BCG." Appellant argues utility for probe, but the specification does not establish the specific utility for what kind of condition is being diagnosed or probed for. Again, as indicated above, "a claim to a polynucleotide whose use is disclosed simply a s a "gene probe" or "chromosome marker" would not be considered to be a specific in the absence of a disclosure of a specific DNA target". Appellant has not clearly defined or disclosed the specific target the polypeptides are used for. It must not be forgotten that "[A]n application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research…an asserted use must show that the claimed invention has a significant and presently available benefit to the public."

The specification does not disclose the actual function of the purified polypeptides that are encoded by the polynucleotide comprising an Open Reading Frame contained within SEQ ID NO: 1. The specification indicates that a polynucleotide of approximately 12.7 kilobases has been isolated that is present in the genome of *M. tuberculosis* but is absent of the genome of *M. bovis* BCG (see paragraph [0063]). Further, the same paragraph discloses that two of the ORFs are of particular interest: ORF6 that encodes a protein that shared significant homology with bacterial GDP-D-mannose dehydratases; the protein encoded by ORF7 shares significant homology with

a nucleotide sugar epimerase (see paragraph [0063]). The specification further discloses that "the highest score was seen with ORF6 whose putative product shows a 51.9% identity with GFP-D-Mannose dehydratase (see paragraph [0238]). Since the sequence homology is only 52%, it is not known whether or not the isolated polypeptide would have similar function as the GDP-D-mannose dehydratase. Further, it is not known where the sequence homology is, i.e., whether the sequence homology is with contiguous amino acid residues or if the homology is spread throughout the sequence. Therefore, the structure of the polypeptide is not known and, thus, the function of the polypeptide is not known. Therefore, without function of the polypeptide, there is no utility. Antigenic properties of the isolated polypeptides are not known. Again, the structure of the isolated polypeptide is not known, and thus, the function of the isolated polypeptide is not known. Without the function of the polypeptide, there is no clear specific and substantial utility.

Furthermore, Appellant makes reference to the written description guidelines. Appellant argues that "assuming that some of the gene products from this region represent proteins with antigenic properties, it could be possible to develop a test that can reliably distinguish between the immune response induced by vaccination with *M. bovis* BCG vaccine strains and infection with *M. tuberculosis*…according to the Office, this assumption is well-grounded. 'Early studies empirically established that proteins were good antigens when injected into a species other than the one from which they originated.'" Appellant argues that "the claimed proteins act as antigens, which can be detected by conventional immunoassays. Their presence indicates the presence of *M.*

tuberculosis regardless of whether or not *M. bovis* is present in the sample." However, having possession does not imply that it has utility. The question presented before in the office actions in this case is not whether the Appellant was in possession of polypeptide of claimed invention but whether the polypeptide of the claimed invention has utility. Establishing written description for the claimed invention does not resolve the utility issue. Utility analysis is distinct from written description analysis for the invention. Furthermore, having written description does not preclude the application from other rejections, such as utility and enablement rejections. Under 35 U.S.C. 112, first paragraph, there are three separate and distinct requirements:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

(A) adequate written description, (B) enablement, and (C) best mode (see MPEP 2106). An application having written description does not imply that the invention has utility or is enabled.

In regards to Appellant's argument that "it is critical to understand that the asserted utility is independent of any homology to GDP-D-mannose dehydratases. This utility derives from the selective presence of one or more claimed polypeptides in one strain of Mycobacterium compared to another strain, and the ability of a conventional assay to distinguish the two strains by the mere presence (or absence) of the polypeptide," the Examiner traverses. Since the structure of the polypeptide is critical to the function of the said polypeptide, the asserted utility is not independent of any

homology to GDP-D-mannose dehydratases. Without the polypeptide function, there is no utility.

In regards to Appellant's argument that "the Examiner failed to consider Appellant's response to the rejection" in that "[R]egardless of the function of the encoded polypeptide...the claimed polynucleotide sequence of the invention had utility simply as a consequence of its expression by *M. tuberculosis*, but not *M. bovis* BCG," the function of the encoded polypeptide is important in determining the utility of the said polypeptide. The mere fact that it can be expressed in a particular system does not mean that it is used in that particular system. Appellant does not specify what the polypeptides are used to diagnose, such as a specific disease, a disorder and so on. The specification does not identify what disease or disorders that the polypeptide would inhibit, which mechanism would be determined by the polypeptide and so on. The specification indicates that the polypeptides are nothing more than research tool, and requires further research to establish "specific and substantial utility". More research must be done to understand the function of the polypeptide, and if any, what the polypeptide can be used to diagnose or probe, since the specification discloses that the polypeptide "may be" used as a probe or a primer. Therefore, the function of the polypeptide is critical to establish specific and substantial utility.

Response to Arguments for Enablement

In regards to Appellant's argument that "the enablement rejection is improper because the utility rejection is improper", no clear specific and substantial utility of the

claimed polypeptide has been established, thus the enablement rejection is proper. The MPEP states the following: "A deficiency under >the utility prong< of 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. See *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995); *In re Jolles*, 628 F.2d 1322, 1326 n.10, 206 USPQ 885, 889, n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) ("If such compositions are in fact useless, appellant's specification cannot have taught how to use them."). Courts have also cast the 35 U.S.C. 101/35 U.S.C. 112 relationship such that 35 U.S.C. 112 presupposes compliance with 35 U.S.C. 101. See *In re Ziegler*, 992 F.2d 1197, 1200-1201, 26 USPQ2d 1600, 1603 (Fed. Cir. 1993) ("The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. 101 that the specification disclose as a matter of fact a practical utility for the invention. …If the application fails as a matter of fact to satisfy 35 U.S.C.§101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112."); *In re Kirk*, 376 F.2d 936, 942, 153 USPQ 48, 53 (CCPA 1967) ("Necessarily, compliance with § 112 requires a description of how to use presently useful invention, otherwise an applicant would anomalously be required to teach how to use a useless invention."). See MPEP 2107.01.

The claimed invention is not supported by a specific and substantial utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. Since the claimed invention is nothing more than a research tool, the claimed polypeptide is

unpredictable. Since the claimed polypeptide is unpredictable (having such a low homology), one of ordinary skill in the art would be burdened with undue experimentation to study if the polypeptides of different sequences would behave similarly to the claimed polypeptide.

Assuming arguendo that the polypeptide has utility, the polypeptide of the invention is not enabled. The polypeptide encoding ORF6 polynucleotide has 51.9% sequence homology to GDP-D-mannose dehydratase. This means, for a GDP-D-mannose dehydratase having 323 amino acid residues, having 51.9% homology implies that a protein has at least 168 amino acids homologous to the wild-type. This means that there are 155 amino acid differences in sequence homology. There are 20 naturally occurring amino acids, thus there would be at least $155^{20} = 6.41 \times 10^{43}$ different peptide sequence possibilities. Further, it is not known if the sequence homology is contiguous or spread throughout within the wild-type sequence. Therefore, the possibilities are vast. A polypeptide having such a vast sequence difference would not necessarily have the same function as the wild-type polypeptide. Since there are vast numbers of the polypeptide sequence homologies available, there is unpredictability in whether the peptide homologs would behave the same way. In other words, since there are only 52% sequence homology to GDP-D-mannose, it is unpredictable to determine which polypeptide having a 52% sequence homology would behave the same way as the wild-type enzyme. The necessary portion of the polypeptide in relation to GDP-D-mannose has not been identified, therefore, there is more unpredictability to the polypeptide sequences. Appellant seems to imply that because of the polypeptides homology to

GDP-D-mannose dehydratase sequence, it can be used for the same purpose. However, due to the unpredictability of the polypeptide function, it lacks enablement. Due to the unpredictability of the polypeptides having the same function as the wild-type enzyme, one of ordinary skill in the art would be burdened with undue experimentation to see which homolog would behave the same way.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Julie Ha/

Examiner, Art Unit 1654

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